PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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New Method in the Biological Diagnosis of Infectious Diseases.—During the past year several articles have appeared dealing with a new method for the diagnosis of infectious diseases, which depends upon a principle apparently of very great importance. It is another application of a method devised by NEISSER and SACHS for the determination, for medico-legal purposes, of the source of specimens of blood. (*Berl. klin. Woch.*, 1905, xlii, 1388.)

If the inactivated blood serum of an animal (for instance, the rabbit), immunized to the blood corpuscles of a second species (say the sheep), is added to a suspension of corpuscles of this second species, hemolysis, of course, occurs when a small amount of fresh, normal serum (guinea-pig, for instance), containing complement, is added. If, however, the fresh normal (guinea-pig) serum (complement containing) be first added to a mixture of the serum of a rabbit immunized to human serum, and then the smallest trace of human serum be added to this, and allowed to stand at 37° C. for a time; and if, then, *this* mixture be added to the above described mixture of corpuscles and immune serum, no hemolysis occurs. If, instead of human serum, or that of an ape, any other kind of serum be added, there is no change in the result; hemolysis goes on as before. In other words, the complement has lost its power to act, by having added to it a mixture of human serum and anti-human serum. It was found that it required only a minimum amount of human serum to carry out this test; 1/10,000 c.c. always sufficed; at times even 1/1,000,000 c.c. was sufficient, and the result was very striking. It is thus seen that the method possesses very decided advantages over the precipitin reaction of Uhlenluth and that of Wassermann and Schütze.

A somewhat similar reaction had previously been described by Moreschi and by Bordet and Gengou, but they did not recognize the application, and explained it in a somewhat different way. Neisser and Sachs think it depends upon a principle first advanced by Ehrlich and Morgenroth, namely, that amboceptors alone are unable to bind complement, but by becoming anchored to the substance used for immunization (antigen) they undergo such an increase in avidity that they are now able to attach the complement. It is this binding of the complement and so its deflection from the corpuscles to which the hemolytic amboceptors are attached, that prevents hemolysis.

It is quite evident that if this principle be correct, we can not only determine the presence of the specific serum in an unknown blood, but on the other hand, given this specific serum, we can determine whether in a second serum anti-bodies for this serum be present or not; in other words the reaction works both ways, either to demonstrate the presence of the antigen (the immunizing substance) or of amboceptors, when either one is known to be present.

Wassermann and Bruck (*Med. Klinik*, 1905, No. 55) now made a wider application of this principle to detect, not specific serum albumins, or their anti-bodies, as in the Neisser-Sachs application, but to detect the presence or absence of minimal quantities of dissolved bacterial substances or of their corresponding anti-bodies or amboceptors. Thus, if to a watery extract of typhoid bacilli, the serum of a patient with typhoid fever and complement-containing serum be added, and if after waiting a short time it be found that the complement has been bound (since it is now no longer able to activate hemolytic sera) we may conclude that in the patient's blood there are present amboceptors corresponding to the dissolved bacterial substances. On the other hand, with this method it is possible to detect small amounts of the bacterial substances in the body-fluids. Thus, if to the serum of a patient, under proper controls, and in varying quantities, the serum of an animal highly immunized to typhoid bacilli (therefore containing amboceptors) be added, and if to this we add fresh complement, if later it be found that the complement is bound (by the method previously described), we may conclude that in the serum of the patient dissolved bacterial substances were present, which were able to unite with the amboceptors. They have found such conditions to occur.

They have applied this method to the study of tuberculosis, especially to the study of the action of tuberculin (*Deut. med. Woch.*, 1906, xxxii, 449). By this method they demonstrated the presence of anti-tuberculin in tuberculous organs. In the blood of untreated patients with pulmonary tuberculosis, however, no anti-tuberculin could be demonstrated. On the other hand, during the course of treatment of tuberculous patients with tuberculin, specific anti-tuberculin appeared in the circulating blood. In a most interesting way they apply their findings to a theoretical discussion of the action of tuberculin, and the theories set forth seem to agree with the facts as known. Since usually the anti-tuberculin is obtained only in the tuberculous organ and not throughout the body, all of the tuberculin must be attached in this situation. This explains why such small doses of tuberculin are active. For instance, suppose a person with lupus reacts to 1 milligram of tuberculin, as is often the case. This small amount, when diluted in the blood of an ordinary sized man, makes a dilution of 1 in 5,000,000 (about). Such a dilution, however, injected directly into a tuberculous focus causes no reaction. The above observation seems to offer a good explanation for this. An explanation for the local reaction, which is manifested by a softening and rendering homogeneous of the tuberculous tissue, is also given. It is supposed that this is due to the fact that by the union of the tuberculin and anti-tuberculin, complement is bound. Now it is known that wherever by means of amboceptors complement is concentrated and active, organic albuminous substances are dissolved, digested. This is to be considered not only due to the action of the free digesting substances obtained by the breaking down of the leukocytes, but also to the digestive power of the leukocytes themselves, which are attracted to the part and which produce the small, round-cell infiltration about the node. The general reaction, the fever, is thought to be due to the absorption of the soluble products of this digestion. The reason, therefore, that the tuberculous react to much smaller doses than the healthy is that only with the former does acute reabsorption occur. If anti-tuberculin were present in the blood in sufficient amounts no reaction would occur. This not infrequently does happen after previous treatment with tuberculin, and explains why persons with relatively fresh tuberculous processes react best. They show, experimentally, that after tuberculin treatment anti-tuberculin appears in the circulating blood, with greatest readiness in cattle, less readily in guinea-pigs, and least readily in man. The fact with regard to cattle has been taken advantage of, so the writers state, by unscrupulous exporters of beef to Germany. By giving cattle a dose of tuberculin before starting, they fail to react to a second dose when they arrive in Germany, even if they are tuberculous. The writers think this is due to the appearance of anti-tuberculin in the blood, and they propose to detect such tuberculous cattle on their arrival at quarantine, not by the tuberculin test, but by the detection of anti-tuberculin in the blood, by the method of complement deflection ("ablenkung").

It is unfortunate, so far as the clinical diagnosis of tuberculosis is concerned, that tuberculin or anti-tuberculin is not present in the blood of the untreated, as in that way a ready method of diagnosis would be at hand. Bruck (*Deutsche med. Woch.*, 1906, xxxii, 945), however, has shown that while this is true for local tuberculosis, in general miliary tuberculosis this is probably not the case, as by the method previously described he was able, in the early days of a case of acute miliary tuberculosis, to detect in the blood specific substances of the tubercle bacillus, and so to make a definite diagnosis at a time when, by previously employed methods, it was not possible to do so. It is of interest that during the course of the disease the reaction disappeared, but at the same time the presence of anti-bodies could be demonstrated. Before exitus, however, these disappeared, and the bacterial substances were again demonstrable. During the period when anti-substances were present, the patient's condition seemed to be better.

Further, by this method Bruck has frequently succeeded in demonstrating the presence of soluble substances of the tubercle bacillus in pleuritic exudates and so determining their nature when this was possible in no other way. Also in the spinal fluid of two cases of cerebrospinal meningitis he was able to detect, by means of a specific meningococcic serum, the presence of meningococcic bacterial substances. So, also, in streptococcic infections analogous specific substances have been detected in the blood.

Lastly, Wassermann, Neisser, and Bruck (*Deutsche med. Woch.*, 1906, xxxii, 745) have applied this method to the study of syphilis, and although the communication is only a preliminary one, it seems to be of very great importance. By proper methods they have produced an immune serum in apes, and have proved by means of complement deflection (1) that in the serum there are present anti-bodies to specific syphilitic substances, and (2) in the extracts of tissues such substances may be demonstrated. This, therefore, offers a possible sero-diagnostic reaction for syphilitic material, and so is of great value in the experimental study of the disease. On the other hand, it offers a method for determining whether in human serum specific substances are present. The tests so far in this direction have been inconclusive, but the power of the immune serum will be of great importance in the successful carrying out of this test, and the writers are at present attempting to obtain as active a serum as possible. If it can be shown that in the circulating blood of luetic patients such substances are always present, the diagnostic importance will be great.

Paralysis of the Recurrent Laryngeal Nerve in Mitral Stenosis.—FIRSCHAUER (*Wien. klin. Woch.*, 1905, xviii, 1383) reports the occurrence of complete paralysis of the left vocal cord in a woman, aged thirty years, with mitral stenosis. At autopsy the left recurrent laryngeal was found compressed and degenerated at the point where it curves under the arch of the aorta and passes between the aorta and the left branch of the pulmonary artery. The left auricle was tremendously dilated and the dilated auricle and engorged pulmonary veins, by pressing the pulmonary artery upward and forward, compromised the nerve between it and the arch of the aorta. Ortner, who was the first to call attention to this relation between mitral stenosis and laryngeal paralysis, published in 1897 two instances in which the paralysis of the recurring nerve was due to direct pressure from the enlarged left auricle. In one instance the left bronchus was pushed forward and lay directly upon the auricle and was itself somewhat flattened. Krauss, in a later publication expressed doubt as to the possibility of the auricle itself ever pressing directly upon the recurrent nerve. But Hofbauer, to sustain Ortner's view, has narrated an instance in which with great hypertrophy of the left auricle the tip appeared between the aorta and the pulmonary artery and at autopsy had to be pulled from between them. In a case reported by Krauss and in another by von Schröter the nerve was pressed upon by the ligamentum botalli. In Krauss' case the ligament ran more directly backward than normal, so that the nerve as it turns to loop about the aorta instead of lying beside it crossed over it, and as the pulmonary artery was pushed upward and forward by the enlarged left auricle the nerve became compressed between the ligament and the left main branch of the pulmonary artery. In von Schröter's case the pulmonary artery was markedly dilated and was larger than the aorta. The ductus botalli was patent, and as large as the main branches of the pulmonic. The recurrent nerve was caught in the outer angle of the point of origin of the ductus and compressed between the distended vessels.

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